Paper No. 24

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte PAUL AVERBACK

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Appeal No. 1999-0494
Application 08/482,768

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ON BRIEF

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Before WILLIAM F. SMITH, ADAMS, and GRIMES Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 13 through 15 and 17 through 21, all the claims pending in the application.

Claims 13, 14, and 15 are representative of the subject matter on appeal and read as follows:

13. A composition comprising (a) a therapeutically effective amount of a compound that inhibits formation of amyloid fibrils when administered, at an in-tissue concentration of about 10^{-5} M or less, to a test animal that has received an intracerebral injection of DMS and (b) a pharmaceutically acceptable carrier, wherein said composition is capable of crossing the blood-brain barrier.

14. The composition as claimed in claim 13, wherein said compound inhibits formation of amyloid fibrils by acting on DMS components such that a structural transition of DMS protein in the brain to a β-pleated sheet conformation is prevented.

15. The composition as claimed in claim 13, wherein said compound is selected from the group consisting of pyrimethamine, cromolyn sodium, erythromycin, purpurogallin, tartrazine, sulfanilamide, benzopurpurine 4B, 29H, 31H-phthalocyanine, 5-methyl-2-thiouridine and 1,2-benzylsoxazole.

The references relied upon by the examiner are:

Haber et al. (Haber)	3,728,452	Apr. 17, 1973
Johnson	4,064,248	Dec. 20, 1977

The Merck Index, Eleventh Edition, page 1264, No. 7963

Claims 13 through 15 stand rejected under 35 U.S.C. § 112, fourth paragraph, as being in improper form. Claims 13 through 15 and 17 through 21 stand rejected under 35 U.S.C. § 103(a). As evidence of obviousness, the examiner relies upon "Merck, Johnson, and Haber." We reverse. In addition, we make a new ground of rejection under the provisions of 37 CFR § 1.196(b).

BACKGROUND

The claimed invention is directed to a composition which comprises a therapeutically effective amount of a compound in a pharmaceutically acceptable carrier. The composition must be capable of crossing a blood-brain barrier. The compound is defined in claims 13 and 14 in a functional manner while claim 15 sets forth a Markush group of compounds which possess the functional requirements of claim 13.

As seen from claim 13, the compound must inhibit formation of amyloid fibrils when administered to a test animal under certain conditions. The conditions include an

intracerebral injection of DMS. DMS is an acronym for "dense microspheres."

Specification, page 4. As explained:

> A microscopic structure referred to as the dense microsphere is known to exist in normal brain and in brain affected by Alzheimer's disease. See Averback, Acta Neuropathol. 61: 148-52 (1983); results confirmed by Hara, J. Neuropath. Exp. Neurol. (1986). Evidence for the existence of dense microspheres (DMS) comes from microscopic histological section studies of fixed whole brain tissue, where the dense microspheres are seen to have a proteinaceous central region ("DMS protein") surrounded by continuous membrane ("DMS membrane"). The dense microspheres are observed as randomly dispersed, very infrequent structures which occupy an estimated 10^{-9} or less of total brain volume, at a unit frequency roughly estimated at 10^{-16} or less, relative to other definable brain structures such as mitochondria.

Id. Appellant believes that development of amyloid fibrils associated with a number of conditions including Alzheimer's disease is tied to the unchecked disruption of DMS in vivo. Specification, page 8. Appellant describes a screening procedure for identifying compounds which inhibit the disruption of DMS in vivo. As explained:

> It has also been discovered that compounds which are effective, at a in-tissue concentration of about 10^{-5} M or less, in impeding the formation of amyloid fibrils in test animals which receive DMS via intracerebral injection can be used to treat cerebral amyloidosis, including Alzheimer's disease. Particularly effective in this regard are compounds that act on DMS protein or DMS membrane, for example, via intracellular or extracellular binding, so as to prevent a structural transition of DMS protein in the brain to a β-pleated sheet conformation.

Specification, page 8, lines 15-26.

Example 2 of the specification describes use of this assay to identify compounds meeting the requirements of claim 13. Of the seven compounds tested in Example 2, appellant states that only three compounds, pyrimethamine, cromolyn sodium, and erythromycin were found to inhibit amyloid formation in vivo at in-tissue levels in the range of 10^{-5} to 10^{-6} M. On the basis of those results, appellant states that those three

compounds are suitable for use in the treatment method of the present invention.

Specification, page 32.

DISCUSSION

1. Rejection under 35 U.S.C. § 112, fourth paragraph

The examiner's reasoning in support of this rejection is:

> The claims relate to the intended use of the composition. Therefore, they are not a proper definition of the composition as they are not limiting of the composition per se.

Examiner's Answer, page 3.

The examiner's statement of the rejection is all but incomprehensible and lacks logic. First, it is not clear why claim 13, an independent claim, is subject to this rejection. Nor is it clear why claim 15 is subject to this rejection as that claim is limited to a Markush group of specific compounds useful in the composition of claim 13.

It appears that the examiner's concern in terms of proper dependency is limited to claim 14. But neither statement by the examiner explains why claim 14 does not serve to further limit claim 13. On its face, claim 14 is directed to a narrower subgenus of compounds than those required by claim 13 in that the compounds of claim 14, besides possessing the property required by claim 13, must also inhibit formation of amyloid fibrils by the activity described in claim 14.

While not clear from the statement of the rejection, it may be the examiner's concern that not all of the compounds described by appellant in the specification possess the properties required by both claims 13 and 14. In other words, appellant may not have described in the specification compounds possessing the property of claim 13 but not the property of claim 14. If so, those question would be properly raised

under the enablement requirement of 35 U.S.C. § 112, first paragraph, not the dependency requirement of the fourth paragraph of this section of the statute.

The examiner's rejection under 35 U.S.C. § 112, fourth paragraph, is reversed.

2. Obviousness

The examiner's facts and reasoning in support of the rejection under this section of the statute are:

> Merck teaches purpurogallin used as a pharmaceutical to retard oxidation, Johnson teaches at column 1, lines 25-30 the use of cromolyn sodium as an antiasthmatic drug and Haber et al at column 1, lines 4-67 teaches the use of pyrimethamine in a pharmaceutical composition. The compositions of claims 13-15 and the mode and means of administration of claims 17-21 are obviated under 35 U.S.C. 103 since an intended use limitation does not render the composition unobvious. See In re Skoner, 186 USPQ 80, (CCPA 1975); In re Kalm 154 USPQ 10 (CCPA 1967); In re Halley 132 USPQ 16 (CCPA 1961).
>
> For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Examiner's Answer, pages 3-4. The examiner further explains the rejection stating "the rejection of claims 13-21 [sic, 13-15, 17-21] under 35 USC 103 (a) is deemed proper since the compositions claimed are taught by the art." Id., page 5.

The examiner's position on appeal as to why the subject matter of any individual claim would have been obvious to one of ordinary skill in the art under this section of the statute is difficult to discern. By the examiner's statement, that the "compositions claimed are taught by the art" bespeaks of an anticipation rejection under 35 U.S.C. § 102, not an obviousness rejection under 35 U.S.C. § 103. Furthermore, the examiner's fact finding is open to question in regard to certain of the applied references. For example, the examiner states that the Merck Index teaches "purpurogallin used as a

pharmaceutical to retard oxidation." The record copy of the Merck Index is difficult to read due to the photocopy supplied by the examiner but it does not appear to use the word "pharmaceutical."

In any event, the examiner's statement of the rejection under 35 U.S.C. § 103(a) is fundamentally deficient in that it does not address the subject matter of the claims as a whole. As seen from claim 13, the composition must be "capable of crossing the blood-brain barrier." Nowhere in the Examiner's Answer does the examiner explain how any of the references relied upon teaches or suggests this aspect of the claimed subject matter.

The examiner's rejection under 35 U.S.C. § 103(a) is reversed.

NEW GROUND OF REJECTION UNDER 37 CFR § 1.196(b)

Under the provisions of 37 CFR § 1.196(b), we make the following new ground of rejection.

Claims 13-15 and 17-21 are rejected under 35 U.S.C. § 102(b). As evidence of anticipation, we rely upon Johnson.

1. Claims 13-15

For ease of explaining the facts and reasoning in support of the new ground of rejection, we will consider these three claims as a group.

In considering claims 13, 14 and 15 together, it is apparent that cromolyn sodium meets the functional requirements of both claims 13 and 14 in terms of inhibiting formation of amyloid fibrils as confirmed by the results of Example 2 of the present specification.

Johnson describes pharmaceutical compositions comprising cromolyn sodium and a pharmaceutically acceptable carrier. See, e.g., column 1, lines 57-66 of Johnson. The question becomes twofold. First, does Johnson describe a cromolyn sodium containing pharmaceutical composition which contains cromolyn sodium in the "therapeutically effective amount" of the claims? Second, is the cromolyn sodium pharmaceutical composition described in Johnson "capable of crossing the blood-brain barrier?"

In regard to the "therapeutically effective amount" language of claim 13 on appeal, we note that the claim does not specifically state what the therapeutic effect of the composition is to be. The claim language regarding inhibiting formation of amyloid fibrils is directed to a property of the active agent, here, cromolyn sodium, not to the amount of the active agent to be present in the composition. Thus, the pharmaceutical composition described in Johnson, of necessity, contains a "therapeutically effective amount" of cromolyn sodium, at least for the purposes described in Johnson. In other words, the "therapeutically effective amount" language of claim 13 does not serve to distinguish the claimed composition from those described in Johnson.

Turning to the other possible point of distinction between the respective compositions, i.e., the requirement of claim 13 that the composition is capable of crossing the blood-brain barrier, we note that Johnson does not discuss this property whatsoever. However, this does not mean that claims 13-15 are patentably distinct from the cromolyn sodium compositions described in Johnson.

Under these circumstances, it is reasonable to shift the burden to applicant to provide evidence establishing in the first instance that the cromolyn sodium

pharmaceutical compositions described in Johnson do not possess this property. As stated in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977):

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on `inherency' under 35 U.S.C. § 102, on `prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

If in future proceedings evidence is provided establishing that the cromolyn sodium pharmaceutical compositions of Johnson do not possess this property, the examiner would need to evaluate Johnson under 35 U.S.C. § 103 in light of other relevant prior art to determine whether the claimed compositions, to the extent that they include cromolyn sodium, would have been obvious. If on the other hand it turns out that the cromolyn sodium pharmaceutical compositions described in Johnson do possess this property, applicant's observation of this property, as opposed to the silence of Johnson, does not mean that the compositions of claims 13-15 are patentable. As stated in In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) (citations omitted) "discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known compositions."

2. Claims 17-21

These claims further limit claim 13 in regard to the pharmaceutically acceptable carrier (claim 17), that the composition be orally, rectally, or nasally acceptable (claims 18-20) and the composition be in spray or aerosol form (claim 21). Johnson describes a

wide range of forms in which the cromolyn sodium compositions of that invention may be administered. Johnson, column 1, line 67 - column 3, lines 22. Specifically, Johnson describes that the cromolyn sodium may be dissolved in water with salt added to provide an isotonic solution. Johnson, column 2, lines 62-65. Johnson also explicitly teaches that the cromolyn sodium compositions may be orally administered or nasally administered in spray or aerosol form. See, e.g., Johnson, column 1, line 67 - column 2, line 12, column 2 line 48-column 3, line 22. While Johnson does not explicitly state that the composition is "rectally acceptable" as required by claim 19, we note that the liquid formulations described in Johnson would appear to be "rectally acceptable" as would any aqueous liquid formulation.

TIME PERIOD FOR RESPONSE

This opinion contains a new ground of rejection pursuant to 37 CFR § 1.196(b). 37 CFR § 1.196(b) provides that, “A new ground of rejection shall not be considered final for purposes of judicial review.”

37 CFR § 1.196(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .
> No time period for taking any subsequent action in connection with this appeal

may be extended under 37 CFR § 1.136(a).

The examiner's decision is reversed.

REVERSED; 196(b)

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William F. Smith	)
Administrative Patent Judge	)
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	)
	) BOARD OF PATENT
Donald E. Adams	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
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Eric Grimes	)
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